FILE 'BIOTECHNO' ENTERED AT 11:23:02 ON 30 MAR 2005

FILE 'CONFSCI' ENTERED AT 11:23:02 ON 30 MAR 2005

FILE 'HEALSAFE' ENTERED AT 11:23:02 ON 30 MAR 2005

FILE 'IMSDRUGCONF' ENTERED AT 11:23:02 ON 30 MAR 2005

FILE 'LIFESCI' ENTERED AT 11:23:02 ON 30 MAR 2005

FILE 'MEDICONF' ENTERED AT 11:23:02 ON 30 MAR 2005

FILE 'PASCAL' ENTERED AT 11:23:02 ON 30 MAR 2005

=> (CAG repeat) and filament
L1 0 FILE AGRICOLA
L2 2 FILE BIOTECHNO
L3 0 FILE CONFSCI
L4 0 FILE HEALSAFE
L5 0 FILE IMSDRUGCONF
L6 2 FILE LIFESCI
L7 0 FILE MEDICONF
L8 4 FILE PASCAL

TOTAL FOR ALL FILES
L9 8 (CAG REPEAT) AND FILAMENT

=> dup rem
ENTER L# LIST OR (END):l9
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L9
L10 7 DUP REM L9 (1 DUPLICATE REMOVED)

=> d l10 ibib abs total

L10 ANSWER 1 OF 7 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 2003:45445 LIFESCI
TITLE: Amyloid-like Features of Polyglutamine Aggregates and Their Assembly Kinetics
AUTHOR: Chen, Songming; Berthelier, V.; Hamilton, J.B.; O'Nuallain, B.; Wetzel, R.
CORPORATE SOURCE: Graduate School of Medicine, University of Tennessee Medical Center, 1924 Alcoa Highway, Knoxville, TN 37920, USA
SOURCE: Biochemistry (Washington) [Biochemistry (Wash.)], (20020611) vol. 41, no. 23, pp. 7391-7399.
ISSN: 0006-2960.
DOCUMENT TYPE: Journal
FILE SEGMENT: N3
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The repeat length-dependent tendency of the polyglutamine sequences of certain proteins to form aggregates may underlie the cytotoxicity of these sequences in expanded **CAG repeat** diseases such as Huntington's disease. We report here a number of features of various

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                  (ROSPATENT) added to list of core patent offices covered
 NEWS  4  FEB 28  PATDPAFULL - New display fields provide for legal status
                  data from INPADOC
 NEWS  5  FEB 28  BABS - Current-awareness alerts (SDIs) available
 NEWS  6  FEB 28  MEDLINE/LMEDLINE reloaded
 NEWS  7  MAR 02  GBFULL: New full-text patent database on STN
 NEWS  8  MAR 03  REGISTRY/ZREGISTRY - Sequence annotations enhanced
 NEWS  9  MAR 03  MEDLINE file segment of TOXCENTER reloaded
 NEWS  10 MAR 22  KOREAPAT now updated monthly; patent information enhanced
 NEWS  11 MAR 22  Original IDE display format returns to REGISTRY/ZREGISTRY
 NEWS  12 MAR 22  PATDPASPC - New patent database available
 NEWS  13 MAR 22  REGISTRY/ZREGISTRY enhanced with experimental property tags

 NEWS EXPRESS  JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
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FILE 'HOME' ENTERED AT 11:22:48 ON 30 MAR 2005

=> file .meeting
'EVENTLINE' IS NOT A VALID FILE NAME
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accessing the remaining file names entered.
ENTER A FILE NAME OR (IGNORE):ignore
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'AGRICOLA' ENTERED AT 11:23:02 ON 30 MAR 2005
```

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	("6153186").PN.	USPAT; EPO	OR	OFF	2005/03/30 10:09
L2	201	polyglutamine near5 repeat	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/03/30 10:09
L3	181	polyglutamine near3 repeat	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/03/30 10:09
L4	42	l3 same aggregate	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/03/30 10:10
L5	6	l3 same aggregate same filament	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/03/30 10:10

polyglutamine (polyGln) aggregates and their assembly pathways that bear a resemblance to generally recognized defining features of amyloid fibrils. PolyGln aggregation kinetics displays concentration and length dependence and a lag phase that can be abbreviated by seeding. PolyGln aggregates exhibit classical beta -sheet-rich circular dichroism spectra consistent with an amyloid-like substructure. The fundamental structural unit of all the in vitro aggregates described here is a **filament** about 3 nm in width, resembling the protofibrillar intermediates in amyloid fibril assembly. We observed these filamentous structures either as isolated threads, as components of ribbonlike sheets, or, rarely, in amyloid-like twisted fibrils. All of the polyGln aggregates described here bind thioflavin T and shift its fluorescence spectrum. Although all polyGln aggregates tested bind the dye Congo red, only aggregates of a relatively long polyGln peptide exhibit Congo red birefringence, and this birefringence is only observed in a small portion of these aggregates. Remarkably, a monoclonal antibody with high selectivity for a generic amyloid fibril conformational epitope is capable of binding polyGln aggregates. Thus, polyGln aggregates exhibit most of the characteristic features of amyloid, but the twisted fibril structure with Congo red birefringence is not the predominant form in the polyGln repeat length range studied here. We also find that polyGln peptides exhibit an unusual freezing-dependent aggregation that appears to be caused by the freeze concentration of peptide and/or buffer components. This is of both fundamental and practical significance. PolyGln aggregation is revealed to be a highly specific process consistent with a significant degree of order in the molecular structure of the product. This ordered structure, or the assembly process leading to it, may be responsible for the cell-specific neuronal degeneration observed in Huntington's and other expanded **CAG repeat** diseases.

L10 ANSWER 2 OF 7 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 2003:36855 LIFESCI
TITLE: A Drosophila Homolog of the Polyglutamine Disease Gene SCA2 Is a Dosage-Sensitive Regulator of Actin **Filament** Formation
AUTHOR: Satterfield, T.F.; Jackson, S.M.; Pallanck, L.J.
CORPORATE SOURCE: University of Washington, Box 357730, Health Sciences Bldg., K-357, Seattle, WA 98195-7730; E-mail: pallanck@gs.washington.edu
SOURCE: Genetics, (20021200) vol. 162, no. 4, pp. 1687-1702. Corresponding author: Leo J. Pallanck. ISSN: 0016-6731.
DOCUMENT TYPE: Journal
FILE SEGMENT: G
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Spinocerebellar ataxia type 2 (SCA2) is a neurodegenerative disorder caused by the expansion of a **CAG repeat** encoding a polyglutamine tract in ataxin- 2, the SCA2 gene product. The normal cellular function of ataxin-2 and the mechanism by which polyglutamine expansion of ataxin-2 causes neurodegeneration remain unknown. In this study we have used genetic and molecular approaches to investigate the function of a Drosophila homolog of the SCA2 gene (Datx2). Like human ataxin-2, Datx2 is found throughout development in a variety of tissue types and localizes to the cytoplasm. Mutations that reduce Datx2 activity or transgenic overexpression of Datx2 result in female sterility, aberrant sensory bristle morphology, loss or degeneration of tissues, and lethality. These phenotypes appear to result from actin **filament** formation defects occurring downstream of actin synthesis. Further studies demonstrate that Datx2 does not assemble with actin **filaments**, suggesting that the role of Datx2 in actin **filament** formation is indirect. These results indicate that Datx2 is a dosage- sensitive regulator of actin **filament** formation. Given that loss of cytoskeleton-dependent dendritic structure defines an early event in SCA2 pathogenesis, our findings suggest the possibility that dysregulation of actin cytoskeletal structure resulting from altered ataxin-2 activity is responsible for neurodegeneration in SCA2.

L10 ANSWER 3 OF 7 PASCAL COPYRIGHT 2005 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000-0295083 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2000 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Ubiquitinated filamentous inclusions in cerebellar dentate nucleus neurons in dentatorubral-pallidoluysian atrophy contain expanded polyglutamine stretches
AUTHOR: YAMADA M.; PIAO Y.-S.; TOYOSHIMA Y.; TSUJI S.; TAKAHASHI H.
CORPORATE SOURCE: Department of Pathology, Brain Research Institute, Niigata University, 1 Asahimachi, Niigata 951-8585, Japan; Department of Neurology, Brain Research Institute, Niigata University, 1 Asahimachi, Niigata 951-8585, Japan
SOURCE: Acta neuropathologica, (2000), 99(6), 615-618, 22 refs.
ISSN: 0001-6322 CODEN: ANPTAL
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
AVAILABILITY: INIST-9757, 354000088487990030
AN 2000-0295083 PASCAL
CP Copyright .COPYRGT. 2000 INIST-CNRS. All rights reserved.
AB We have recently reported that, in addition to the widespread occurrence of ubiquitinated neuronal intranuclear inclusions (NIIs), the restricted occurrence of ubiquitinated intracytoplasmic filamentous inclusions in the neurons of the cerebellar dentate nucleus (CDN) is a characteristic feature of dentatorubral-pallidoluysian atrophy (DRPLA). Interestingly, these neuronal intracytoplasmic filamentous inclusions (NIFIs) were morphologically indistinguishable from the skein-like inclusions (SLIs) described previously in the spinal anterior horn cells in amyotrophic lateral sclerosis (ALS). In the present study, we examined immunohistochemically the CDN in ten patients with clinicopathologically and genetically confirmed DRPLA and the spinal anterior horns in five patients with sporadic ALS, using a monoclonal antibody (1C2) directed against long polyglutamine stretches. In all of the patients with DRPLA, both the NIFIs and the Nils were visualized clearly with 1C2. Conversely, in the patients with ALS all structures, including the SLIs, were completely negative. These findings indicate that in DRPLA, the NIFIs in the CDN are an alteration that is directly related to the causative gene abnormality (an expanded **CAG repeat** encoding polyglutamine) and that, from the molecular point of view, they are distinct from the SLIs in ALS.

L10 ANSWER 4 OF 7 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2000:30825603 BIOTECHNO
TITLE: Molecular characterization of human tensin
AUTHOR: Chen H.; Ishii A.; Wong W.-K.; Chen L.B.; Lo S.H.
CORPORATE SOURCE: S.H. Lo, Ctr. for Tissue Regeneration/Repair, Department of Orthopaedic Surgery, University of California-Davis, 4635 Second Avenue, Sacramento, CA 95817, United States.
E-mail: shlo@ucdavis.edu
SOURCE: Biochemical Journal, (15 OCT 2000), 351/2 (403-411), 46 reference(s)
CODEN: BIJOAK ISSN: 0264-6021
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2000:30825603 BIOTECHNO
AB Tensin is a focal-adhesion molecule that binds to actin **filaments** and interacts with phosphotyrosine-containing proteins. To analyse tensin's function in mammals, we have cloned tensin cDNAs from human and cow. The isolated approx. 7.7-kb human cDNA contains an open reading

frame encoding 1735 amino acid residues. The amino acid sequence of human tensin shares 60% identity with chicken tensin, and contains all the structural features described previously in chicken tensin. This includes the actin-binding domains, the Src homology domain 2, and the region similar to a tumour suppressor, PTEN. Two major differences between human and chicken tensin are (i) the lack of the first 54 residues present in chicken tensin, and (ii) the addition of 34- and 38-residue inserts in human and bovine tensin. In addition, our interspecies sequencing data have uncovered the presence of a glutamine/**CAG repeat** that appears to have expanded in the course of evolution. Northern-blot analysis reveals a 10-kb message in most of the human tissues examined. An additional 9-kb message is detected in heart and skeletal muscles. The molecular mass predicted from the human cDNA is 185 kDa, although both endogenous and recombinant human tensin migrate as 220-kDa proteins on SDS/PAGE. The discrepancy is due to the unusually low electrophoretic mobility of the central region of the tensin polypeptide (residues 306-981). A survey of human prostate and breast cancer cell lines by Western-blot analysis shows a lack of tensin expression in most cancer cell lines, whereas these lines express considerable amounts of focal-adhesion molecules such as talin and focal-adhesion kinase. Finally, tensin is rapidly cleaved by a focal-adhesion protease, calpain II. Incubation of cells with a calpain inhibitor, MDL, prevented tensin cleavage and induced morphological change in these cells, suggesting that cleavage of tensin and other focal-adhesion constituents by calpain disrupts maintenance of normal cell shape.

L10 ANSWER 5 OF 7 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 1999:29124713 BIOTECHNO
TITLE: Expanded polyglutamine domain proteins bind neurofilament and alter the neurofilament network
AUTHOR: Nagai Y.; Onodera O.; Chun J.; Strittmatter W.J.; Burke J.R.
CORPORATE SOURCE: J.R. Burke, Department of Medicine (Neurology), Deane Laboratory, Duke University Medical Center, Durham, NC 27710, United States.
E-mail: james.burke@duke.edu
SOURCE: Experimental Neurology, (1999), 155/2 (195-203), 50 reference(s)
CODEN: EXNEAC ISSN: 0014-4886
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 1999:29124713 BIOTECHNO
AB Eight inherited neurodegenerative diseases are caused by genes with expanded **CAG repeats** coding for polyglutamine domains in the disease- producing proteins. The mechanism by which this expanded polyglutamine domain causes neurodegenerative disease is unknown, but nuclear and cytoplasmic polyglutamine protein aggregation is a common feature. In transfected COS7 cells, expanded polyglutamine proteins aggregate and disrupt the vimentin intermediate **filament** network. Since neurons have an intermediate **filament** network composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic-length polyglutamine domain proteins also interact with NF. We expressed varying lengths polyglutamine-green fluorescent protein fusion proteins in a neuroblast cell line, TR1. Pathologic-length polyglutamine-GFP fusion proteins formed large cytoplasmic aggregates surrounded by neurofilament. Immunoisolation of pathologic-length polyglutamine proteins coisolated 68- kDa NF protein demonstrating molecular interaction. These observations suggest that polyglutamine interaction with NF is important in the pathogenesis of the polyglutamine repeat diseases.

L10 ANSWER 6 OF 7 PASCAL COPYRIGHT 2005 INIST-CNRS. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1998-0237652 PASCAL

reserved.
TITLE (IN ENGLISH): Hereditary dentatorubral-pallidoluysian atrophy : ubiquitinated filamentous inclusions in the cerebellar dentate nucleus neurons
AUTHOR: HAYASHI Y.; KAKITA A.; YAMADA M.; EGAWA S.; OYANAGI S.; NAITO H.; TSUJI S.; TAKAHASHI H.
CORPORATE SOURCE: Department of Pathology, Brain Research Institute, Niigata University, 1-757 Asahimachi, Niigata 951-8585, Japan; Department of Neurology, Brain Research Institute, Niigata University, 1-757 Asahimachi, Niigata 951-8585, Japan; Nagaoka Ryoikuen, Fukazawa-cho, Nagaoka, Japan; Matsuhama Hospital, Matsuhama-cho, Niigata, Japan
SOURCE: Acta neuropathologica, (1998), 95(5), 479-482, 25 refs.
ISSN: 0001-6322 CODEN: ANPTAL
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
AVAILABILITY: INIST-9757, 354000075470040060
AN 1998-0237652 PASCAL
CP Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved.
AB We examined the cerebellar dentate nucleus (CDN) in 16 patients with hereditary dentatorubral-pallidoluysian atrophy (DRPLA), one of the neurodegenerative diseases caused by expansion of a **CAG repeat** encoding a polyglutamine tract in the disease protein. In all patients, some CDN neurons were found to contain ubiquitinated filamentous inclusions in their cytoplasm. On hematoxylin and eosin preparations, these filamentous inclusions were eosinophilic, basophilic or amphophilic, and were often found in areas of pale cytoplasm. Electron microscopy revealed that they consisted of bundles of **filaments** that were somewhat thicker than neurofilaments. These features of the present inclusions were indistinguishable from those of skein-like inclusions (SLI) previously described in the lower motor neurons in sporadic amyotrophic lateral sclerosis. We conclude that SLI can also occur in the CDN in DRPLA and believe that they reflect a characteristic pathological process in this disease.

L10 ANSWER 7 OF 7 PASCAL COPYRIGHT 2005 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1998-0270026 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Huntingtin protein colocalizes with lesions of neurodegenerative diseases : An investigation in Huntington's, alzheimer's, and pick's diseases
AUTHOR: SINGHRAO S. K.; THOMAS P.; WOOD J. D.; MACMILLAN J. C.; NEAL J. W.; HARPER P. S.; JONES A. L.
CORPORATE SOURCE: Department of Medical Biochemistry, University of Wales College of Medicine, Heath Park, Cardiff, CF4 4XN, United Kingdom; Institute of Medical Genetics, University of Wales College of Medicine, Heath Park, Cardiff, CF4 4XN, United Kingdom; Neuropathology Laboratory, Department of Pathology, University of Wales College of Medicine, Heath Park, Cardiff, CF4 4XN, United Kingdom
SOURCE: Experimental neurology, (1998), 150(2), 213-222, 52 refs.
ISSN: 0014-4886 CODEN: EXNEAC
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-9181, 354000075540180050
AN 1998-0270026 PASCAL
CP Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved.
AB Huntington's disease (HD) is an autosomal dominant neurodegenerative

disease associated with a CAG trinucleotide repeat expansion in a large gene on chromosome 4. The gene encodes the protein huntingtin with a polyglutamine tract encoded by the **CAG repeat** at the N-terminus. The number of **CAG repeats** in HD are significantly increased (36 to 120+) compared with the normal population (8-39). The pathological mechanism associated with the expanded **CAG repeat** in HD is not clear but there is evidence that polyglutamine is directly neurotoxic. We have immunolocalized huntingtin with an in-house, well-characterised, polyclonal antibody in HD, Alzheimer's disease (AD), and Picks disease (PiD) brains. Control brain tissue sections were from head injured and cerebral ischaemia cases. In HD, huntingtin was immunopositive in the surviving but damaged neurons and reactive astrocytes of the caudate and putamen. However, in AD and PiD the immunostaining was largely restricted to the characteristic intracellular inclusion bodies associated with the disease process in each case. In AD, huntingtin was localized only in the intracellular neurofibrillary tangles and dystrophic neurites within the neuritic amyloid plaques but not with the amyloid. In PiD, strongly positive huntingtin immunostaining was present within cytoplasmic Pick bodies. Our findings suggest huntingtin selectively accumulates in association with abnormal intracytoplasmic and cytoskeletal **filaments** of neurons and glia in neurodegenerative diseases such as HD, AD, and PiD. Cells in the CNS appear sensitive to damage by the aggregated, toxic levels of huntingtin and evidence of its interaction with neurofilaments could provide information about its potential role in the aetiology of HD.

```
=> (polyglutamine)(3A)(repeat)
L11           1 FILE AGRICOLA
L12         164 FILE BIOTECHNO
L13           6 FILE CONFSCI
L14           0 FILE HEALSAFE
L15           0 FILE IMSDRUGCONF
L16         168 FILE LIFESCI
L17           5 FILE MEDICONF
L18         127 FILE PASCAL

TOTAL FOR ALL FILES
L19         471 (POLYGLUTAMINE)(3A)(REPEAT)

=> ((polyglutamine)(3A)(repeat))(P)filament
L20           0 FILE AGRICOLA
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'REPEAT))(P)FILAMENT'
L21           2 FILE BIOTECHNO
L22           0 FILE CONFSCI
L23           0 FILE HEALSAFE
L24           0 FILE IMSDRUGCONF
L25           1 FILE LIFESCI
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'REPEAT))(P)FILAMENT'
L26           0 FILE MEDICONF
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'REPEAT))(P)FILAMENT'
L27           3 FILE PASCAL

TOTAL FOR ALL FILES
L28           6 ((POLYGLUTAMINE)(3A)(REPEAT))(P) FILAMENT

=> dup rem
ENTER L# LIST OR (END):l28
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L28
L29            5 DUP REM L28 (1 DUPLICATE REMOVED)

=> d l29 ibib abs total
```

L29 ANSWER 1 OF 5 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 2003:36855 LIFESCI
TITLE: A Drosophila Homolog of the Polyglutamine Disease Gene SCA2 Is a Dosage-Sensitive Regulator of Actin Filament Formation
AUTHOR: Satterfield, T.F.; Jackson, S.M.; Pallanck, L.J.
CORPORATE SOURCE: University of Washington, Box 357730, Health Sciences Bldg., K-357, Seattle, WA 98195-7730; E-mail: pallanck@gs.washington.edu
SOURCE: Genetics, (20021200) vol. 162, no. 4, pp. 1687-1702. Corresponding author: Leo J. Pallanck. ISSN: 0016-6731.
DOCUMENT TYPE: Journal
FILE SEGMENT: G
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Spinocerebellar ataxia type 2 (SCA2) is a neurodegenerative disorder caused by the expansion of a CAG **repeat** encoding a **polyglutamine** tract in ataxin- 2, the SCA2 gene product. The normal cellular function of ataxin-2 and the mechanism by which polyglutamine expansion of ataxin-2 causes neurodegeneration remain unknown. In this study we have used genetic and molecular approaches to investigate the function of a Drosophila homolog of the SCA2 gene (Datx2). Like human ataxin-2, Datx2 is found throughout development in a variety of tissue types and localizes to the cytoplasm. Mutations that reduce Datx2 activity or transgenic overexpression of Datx2 result in female sterility, aberrant sensory bristle morphology, loss or degeneration of tissues, and lethality. These phenotypes appear to result from actin **filament** formation defects occurring downstream of actin synthesis. Further studies demonstrate that Datx2 does not assemble with actin **filaments**, suggesting that the role of Datx2 in actin **filament** formation is indirect. These results indicate that Datx2 is a dosage- sensitive regulator of actin **filament** formation. Given that loss of cytoskeleton-dependent dendritic structure defines an early event in SCA2 pathogenesis, our findings suggest the possibility that dysregulation of actin cytoskeletal structure resulting from altered ataxin-2 activity is responsible for neurodegeneration in SCA2.

L29 ANSWER 2 OF 5 PASCAL COPYRIGHT 2005 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000-0295083 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2000 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Ubiquitinated filamentous inclusions in cerebellar dentate nucleus neurons in dentatorubral-pallidoluysian atrophy contain expanded polyglutamine stretches
AUTHOR: YAMADA M.; PIAO Y.-S.; TOYOSHIMA Y.; TSUJI S.; TAKAHASHI H.
CORPORATE SOURCE: Department of Pathology, Brain Research Institute, Niigata University, 1 Asahimachi, Niigata 951-8585, Japan; Department of Neurology, Brain Research Institute, Niigata University, 1 Asahimachi, Niigata 951-8585, Japan
SOURCE: Acta neuropathologica, (2000), 99(6), 615-618, 22 refs. ISSN: 0001-6322 CODEN: ANPTAL
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
AVAILABILITY: INIST-9757, 354000088487990030
AN 2000-0295083 PASCAL
CP Copyright .COPYRGT. 2000 INIST-CNRS. All rights reserved.
AB We have recently reported that, in addition to the widespread occurrence of ubiquitinated neuronal intranuclear inclusions (NIIs), the restricted occurrence of ubiquitinated intracytoplasmic filamentous inclusions in the neurons of the cerebellar dentate nucleus (CDN) is a characteristic

feature of dentatorubral-pallidoluysian atrophy (DRPLA). Interestingly, these neuronal intracytoplasmic filamentous inclusions (NIFIs) were morphologically indistinguishable from the skein-like inclusions (SLIs) described previously in the spinal anterior horn cells in amyotrophic lateral sclerosis (ALS). In the present study, we examined immunohistochemically the CDN in ten patients with clinicopathologically and genetically confirmed DRPLA and the spinal anterior horns in five patients with sporadic ALS, using a monoclonal antibody (1C2) directed against long polyglutamine stretches. In all of the patients with DRPLA, both the NIFIs and the Nils were visualized clearly with 1C2. Conversely, in the patients with ALS all structures, including the SLIs, were completely negative. These findings indicate that in DRPLA, the NIFIs in the CDN are an alteration that is directly related to the causative gene abnormality (an expanded CAG **repeat** encoding **polyglutamine**) and that, from the molecular point of view, they are distinct from the SLIs in ALS.

L29 ANSWER 3 OF 5 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE
ACCESSION NUMBER: 1999:29124713 BIOTECHNO
TITLE: Expanded polyglutamine domain proteins bind neurofilament and alter the neurofilament network
AUTHOR: Nagai Y.; Onodera O.; Chun J.; Strittmatter W.J.; Burke J.R.
CORPORATE SOURCE: J.R. Burke, Department of Medicine (Neurology), Deane Laboratory, Duke University Medical Center, Durham, NC 27710, United States.
E-mail: james.burke@duke.edu
SOURCE: Experimental Neurology, (1999), 155/2 (195-203), 50 reference(s)
CODEN: EXNEAC ISSN: 0014-4886
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1999:29124713 BIOTECHNO
AB Eight inherited neurodegenerative diseases are caused by genes with expanded CAG **repeats** coding for **polyglutamine** domains in the disease- producing proteins. The mechanism by which this expanded polyglutamine domain causes neurodegenerative disease is unknown, but nuclear and cytoplasmic polyglutamine protein aggregation is a common feature. In transfected COS7 cells, expanded polyglutamine proteins aggregate and disrupt the vimentin intermediate **filament** network. Since neurons have an intermediate **filament** network composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic-length polyglutamine domain proteins also interact with NF. We expressed varying lengths polyglutamine-green fluorescent protein fusion proteins in a neuroblast cell line, TR1. Pathologic-length polyglutamine-GFP fusion proteins formed large cytoplasmic aggregates surrounded by neurofilament. Immunoisolation of pathologic-length polyglutamine proteins coisolated 68- kDa NF protein demonstrating molecular interaction. These observations suggest that polyglutamine interaction with NF is important in the pathogenesis of the **polyglutamine repeat** diseases.

L29 ANSWER 4 OF 5 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1999:30038076 BIOTECHNO
TITLE: Polyglutamine domain proteins with expanded repeats bind neurofilament, altering the neurofilament network
AUTHOR: Nagai Y.; Onodera O.; Strittmatter W.J.; Burke J.R.
CORPORATE SOURCE: J.R. Burke, Department of Medicine, Duke University Medical Center, Durham, NC 27710, United States.
E-mail: james.burke@duke.edu
SOURCE: Annals of the New York Academy of Sciences, (1999), 893/- (192-202), 49 reference(s)
CODEN: ANYAA0 ISSN: 0077-8923
DOCUMENT TYPE: Journal; Conference Article

COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1999:30038076 BIOTECHNO
AB Proteins with expanded **polyglutamine** (polyQ) **repeats** cause eight inherited neurodegenerative diseases. Nuclear and cytoplasmic polyQ protein is a common feature of these diseases, but its role in cell death remains debatable. Since the neuronal intermediate **filament** network is composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic length polyQ domain proteins interact with NF. We expressed polyQ-green fluorescent fusion proteins (GFP) in a neuroblast cell line, TR1. Pathologic-length polyQ-GFP fusion proteins form large cytoplasmic aggregates surrounded by neurofilament. Immunoisolation of pathologic length polyQ proteins co-isolated 68 kD NF protein demonstrating molecular interaction. These observations suggest that polyQ interaction with NF is important in the pathogenesis of the **polyglutamine repeat** diseases.

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AB We examined the cerebellar dentate nucleus (CDN) in 16 patients with hereditary dentatorubral-pallidoluysian atrophy (DRPLA), one of the neurodegenerative diseases caused by expansion of a CAG **repeat** encoding a **polyglutamine** tract in the disease protein. In all patients, some CDN neurons were found to contain ubiquitinated filamentous inclusions in their cytoplasm. On hematoxylin and eosin preparations, these filamentous inclusions were eosinophilic, basophilic or amphophilic, and were often found in areas of pale cytoplasm. Electron microscopy revealed that they consisted of bundles of **filaments** that were somewhat thicker than neurofilaments. These features of the present inclusions were indistinguishable from those of skein-like inclusions (SLI) previously described in the lower motor neurons in sporadic amyotrophic lateral sclerosis. We conclude that SLI can also occur in the CDN in DRPLA and believe that they reflect a characteristic pathological process in this disease.